REMARKS

Claims 1, 4-9, 16-17, 19-20, 23-26, 31-41, 64 and 65 are pending after submission of this paper. Claims 42-63 have been cancelled. Claims 2-3, 10-15, 18, 21-22, 27-30, and 66-69 are withdrawn. Applicants reserve the right to prosecute the subject matter of the cancelled and withdrawn claims in one or more continuation, continuation-in-part, or divisional applications. Claims 38 and 40 have been amended. No new matter is introduced by these amendments and the amendments are supported by the instant specification.

Response to 35 U.S.C. §112. second paragraph, Rejections

Claims 38, 40, and 41 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner states that these claims are drawn to a method of treating a patient prior to a myocardial infarction and that they are dependent on claims where the myocardial infarction has already occurred.

Applicants have amended claims 38 and 40 to further clarify the claimed subject matter and remedy any inconsistencies. No new matter is introduced by these amendments. Applicants believe that these amendments address the Examiner's rejection and render such rejection moot.

Reconsideration and withdrawal of the rejections under 35 U.S.C. §112, second paragraph, as to claims 38, 40, and 41 are respectfully requested in view of the claim amendments.

Response to 35 U.S.C. §103(a) Rejections

Claims 1, 6-9, and 20 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Hope, et al. (U.S. 6,139,871). Applicants respectfully disagree with this rejection.

Hope describes liposome formulations for the treatment of atherosclerosis. The Examiner takes the position that it would be obvious to one skilled in the art to apply the teachings of Hope to treat acute myocardial infarction (AMI). However, applicants respectfully point out that one skilled in the art would not apply the Hope reference for the treatment of AMI because the action of the formulations taught in Hope cannot directly treat AMI, even though they may be useful as a treatment for atherosclerosis. AMI is an acute life-threatening condition that causes permanent (if not fatal) damage to the heart muscle due to the short-term lack of oxygen to that muscle. Atherosclerosis, on the other hand, is a slow-progressive disease which causes build-up of plaque in the blood vessels. While the examiner correctly points out that the two pathologies are related in as much as atherosclerosis may lead to AMI, we point out that the site of action for the intervention is completely different. Atherosclerosis is a disease of the blood vessels whereas AMI is a pathology caused in the heart muscle (the myocardium) itself. The timing is also completely different. While atherosclerosis may lead to AMI in the long run, once AMI has occurred, it is too late to treat it by treating the underlying atherosclerotic disease.

The Examiner's reliance on the Hope reference for its description of liposomal preparations to treat atherosclerosis thereby reducing plaque build-up in blood vessels is misplaced. To illustrate this point, applicants offer the following analogy: The skilled

artisan would not treat lung cancer by placing a nicotine patch on a patient's chest. This is true despite the fact that a nicotine patch may help one to stop smoking which is the actual direct cause of lung cancer. Similarly, it is too late to treat a patient for atherosclerosis, as taught by Hope, once the patient has an acute myocardial infarction. In addition, Hope does not teach or suggest use of its compositions for treatment of AMI. To be clear, once an acute myocardial event occurs, damage to the heart is caused by a cascade of events including reperfusion of blood into a part of the heart which has been blocked off for a time by the occlusion and has become oxygen starved (*i.e.*, ischemic). Hope does not teach or suggest that its method or composition can reduce or prevent the heart muscle damage resulting from AMI.

Hope describes using liposomal compositions to remove cholesterol to prevent or treat atherosclerotic plaques. However, Hope does not teach or suggest that their compositions can treat heart muscle damage (such as reducing the zone of infarct) once AMI has occurred, as claimed. Applicants assert that the instant claims provide novel methods and compositions to treat AMI and enable the enhanced prevention and/or reduction of ischemic damage which is not taught or suggested by Hope. The instant claims relate to blocking/ameliorating the damage resulting from an acute AMI event (see paragraphs 4-7 of the published specification). Hope does not teach the treatment of AMI and does not teach or suggest that their compositions can effect the permanent damage associated with an AMI event.

Reconsideration and withdrawal of the rejections under 35 U.S.C. §103(a) as to claims 1, 6-9, and 20 are respectfully requested for the above reasons and in view of the claim amendments.

Ylitalo in view of Hope, et al.

Claims 1, 4-9, 16-17, 19, 20, 23-26, 31-38, 40, 41, 64, and 65 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Ylitalo (*Gen. Pharmacol.*, 35:287-296, 2002) in view of Hope, et al. (U.S. 6,139,871). Applicants respectfully disagree with this rejection.

An invention is obvious if the prior art suggests the invention, or if one of ordinary skill in the art would have had a reasonable expectation that the claimed invention would be successful based on the teachings of the prior art. *In re O'Farrell*, 853 F.2d 894, 902-4 (Fed. Cir. 1988); *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q. 2d 1438 (Fed. Cir. 1991). There must be an expectation that the claimed invention will be successful in view of the prior art, and not based on the disclosure of the claimed invention. *In re Dow Chemical Co.,* 5 U.S.P.Q. 2d 1529 (Fed. Cir. 1988). In determining obviousness, "the inquiry is not whether each element existed in prior art, but whether the prior art made obvious the invention as a whole for which patentability is claimed." *Hartness International Inc. v. Simplimatic Engineering Co.,* 819 F.2d 1100, 2 U.S.P.Q. 2d 1826 (Fed. Cir. 1987). This standard is still the law today in view of the recent Supreme Court decision in *KSR Int'l Co. v. Teleflex, Inc.* ___S.C. ___ (Slip Op. April 30, 2007).

Ylitalo describes liposomal formulations of bisphosphonates for the treatment of atherosclerosis by suppressing subendothelial lipid phagocyting cells. However, neither Ylitalo nor Hope teaches or suggest to the skilled artisan that their compositions or methods could be useful to treat the injury resulting from AMI. The treatments

described in Ylitalo and Hope are directed to treating and preventing atherosclerosis by preventing blockages in a blood vessel. Ylitalo describes that bisphosphonates accumulate in the arterial wall and act on cells and calcium channels within this area to reduce the build-up of plaques in the treatment of atherosclerosis (see pages 292-293). Neither Ylitalo nor Hope teach or suggest any methods of treating AMI once it has occurred, nor do these references teach or suggest methods of reducing a zone of infarct, one of the cascades of events that cause damage to the myocardium during an AMI event.

The Ylitalo and Hope references provide no teaching or suggestion that their methods or compositions can treat the damage resulting from AMI or that such treatment can effect the zone of infarct resulting from AMI, as claimed in the instant application. AMI and atherosclerosis are two completely separate and different diseases. They occur at different times, in different places in the body, by different processes and are mediated by different cells. The argument that Ylitalo and Hope describe methods of treating AMI by reducing plaque build-up places the proverbial cart before the horse. While these methods ultimately reduce the likelihood of an AMI event by reducing the plaque build-up within vessels, the references provide no teaching or suggestion that they can be used to treat AMI or can reduce the zone of infarct following an AMI event.

Reconsideration and withdrawal of the rejections under 35 U.S.C. §103(a) as to claims 1, 4-9, 16-17, 19, 20, 23-26, 31-38, 40, 41, 64, and 65 are respectfully requested for the above reasons and in view of the claim amendments.

Golomb, et al. (U.S. 6,719,998) in view of Hope, et al.

Claims 1, 4-9, 16-17, 19, 20, 23-26, 31-41, 64, and 65 have been rejected under 35 U.S.C. §103(a) as being obvious over Golomb, et al. (U.S. 6,719,998) in view of Hope, et al. (U.S. 6,139,871). Applicants respectfully disagree.

Golomb describes a composition for the prevention or treatment of vascular restenosis. The composition in Golomb incorporates a pharmaceutically active ingredient which is combined with a pharmaceutically acceptable carrier, *i.e.* a liposome preparation (see col. 3, lines 1-7; and col. 4, lines 14-24), for the prevention and treatment of restenosis. Restenosis is a condition that involves the re-blockage of a blood vessel after it has been treated to reopen the vessel. The Golomb reference does not teach or suggest a method of treating an acute myocardial infarction or reducing the zone of infarct as claimed. The Golomb reference does not teach or suggest its methods or composition for the treatment of AMI. Although the method described in Golomb may reduce the likelihood of an AMI event by reducing the plaque build-up within vessels, Golomb does not teach or suggest treatments for the AMI event itself or the damage incurred by the event, such as myocardial damage.

Similarly, combining the Golomb reference with the Hope reference also does not reach the presently claimed invention, because neither reference taken alone or in combination teach or suggest a method of treating an acute myocardial infarction or the myocardial damage that results from the AMI. Section 706/02(j) of the MPEP states that "the prior art reference (or references when combined) must teach or suggest all

the claim limitations." As described above, Hope fails to disclose a method or composition for preventing myocardial damage that occurs in an AMI. In addition, Hope does not teach or suggest the treatment of AMI or that its compositions can directly effect AMI-associated permanent damage once AMI has occurred. Golomb does not make up for this deficiency. Neither Golomb nor Hope teach or suggest methods of treating AMI or methods to reduce a zone of infarct, one of the events that can cause damage following an AMI event.

Reconsideration and withdrawal of the rejections under 35 U.S.C. §103(a) as to claims 1, 4-9, 16-17, 19, 20, 23-26, 31-41, 64, and 65 are respectfully requested for the above reasons and in view of the claim amendments.

Golomb, et al. (U.S. 6,984,400) in view of Hope, et al.

Claims 1, 4-9, 16-17, 19, 20, 23-26, 31-41, 64, and 65 have been rejected under 35 U.S.C. §103(a) as being obvious over Golomb, et al. (U.S. 6,984,400) in view of Hope, et al. (U.S. 6,139,871). Applicants respectfully disagree.

Golomb describes a method of treating restenosis by administering an active ingredient with a bisphosphonate particle or a bisphosphonate particulate. This Golomb reference also does not teach or suggest how to treat an acute myocardial infarction or the zone of infarct. Although the method described in Golomb may reduce the likelihood of an AMI event by reducing the plaque build-up within vessels, Golomb does not teach or suggest a method or composition to treat an AMI event or how to treat the zone of infarct following an AMI event where the area has suffered myocardial damage.

Section 706/02(j) of the MPEP states that "the prior art reference (or references when combined) must teach or suggest all the claim limitations." As described above, Hope does not teach or suggest a method or composition that can treat and/or reduce damage to a reperfused area that occurs following an AMI event. Also stated above, Hope does not teach or suggest a method of treating AMI and does not teach or suggest that their compositions can directly effect AMI-associated permanent damage. Golomb does not make up for this deficiency. Neither Golomb nor Hope teach or suggest methods of treating AMI or methods to reduce a zone of infarct, one of the events that can cause damage following an AMI event.

Reconsideration and withdrawal of the rejections under 35 U.S.C. §103(a) as to claims 1, 4-9, 16-17, 19, 20, 23-26, 31-41, 64, and 65 are respectfully requested for the above reasons and in view of the claim amendments.

Golomb, et al. (U.S. 7,008,645)

Claims 1, 4-9, 16-17, 19, 20, 23-26, 31-41, 64, and 65 have been rejected under 35 U.S.C. §103(a) as being obvious over Golomb, et al. (U.S. 7,008,645). Applicants respectfully disagree.

Golomb describes a method of treating restenosis by inhibiting the activity or production of cytokines or growth factors. This Golomb reference also does not teach or suggest how to treat an acute myocardial event nor does it teach or suggest a method or composition capable of reducing the zone of infarct resulting from an AMI. Nothing in the Golomb reference provides the skilled artisan with the teaching or

suggestion that methods of preventing restenosis can be used to treat the zone of infarct following an AMI event where the area has suffered myocardial damage.

Section 706/02(j) of the MPEP states that "the prior art reference (or references when combined) must teach or suggest all the claim limitations." As described above, Hope fails to teach or suggest a method or composition for reducing the myocardial damage that occurs in an AMI. As stated above, Hope does not teach or suggest a method of treating AMI and does not teach or suggest that their compositions can directly effect AMI-associated permanent damage. Golomb does not make up for this deficiency. Neither Golomb nor Hope teach or suggest methods of treating AMI or methods to reduce a zone of infarct, one of the events that can cause damage following an AMI event.

Reconsideration and withdrawal of the rejections under 35 U.S.C. §103(a) as to claims 1, 4-9, 16-17, 19, 20, 23-26, 31-41, 64, and 65 are respectfully requested for the above reasons and in view of the claim amendments.

CONCLUSION

Based on the foregoing amendments and remarks, applicants respectfully request reconsideration and withdrawal of the rejection of claims and allowance of this application.

AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Amendment to Deposit Account No. **13-4500**, Order No. 4313-4005.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. **13-4500**, Order No. 4313-4005.

Respectfully submitted,
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Dated: May 4, 2007

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